

## WHAT IS CLAIMED IS:

1. A synthetic mammalian expression plasmid comprising:
  - (a) a synthetic or eukaryotic promoter;
  - (b) a codon-optimized-eukaryotic therapeutic gene sequence;
  - (c) a poly adenelation signal;
  - (d) a selectable marker gene promoter;
  - (e) a ribosomal binding site;
  - (f) selectable marker gene sequence; and
  - (g) an origin of replication;

wherein the synthetic or eukaryotic promoter, the codon-optimized-eukaryotic therapeutic gene sequence, and the poly adenylation signal comprise therapeutic elements of the synthetic mammalian expression plasmid; the therapeutic elements are operatively linked and located in a first operatively-linked arrangement; the selectable marker gene promoter, the ribosomal binding site, the selectable marker gene sequence, and the origin of replication comprise replication elements of the synthetic mammalian expression plasmid; the replication elements are operatively linked and located in a second operatively-linked arrangement; the first-operatively-linked arrangement and the second-operatively-linked arrangement comprise a circular structure of the synthetic mammalian expression plasmid; and the synthetic mammalian expression plasmid is utilized for plasmid mediated gene supplementation.

2. The synthetic mammalian expression plasmid of claim 1, wherein the origin of replication comprises a prokaryotic origin of replication sequence.
3. The synthetic mammalian expression plasmid of claim 1, wherein the origin of replication comprises an autonomously replication sequence ("ARS").
4. The synthetic mammalian expression plasmid of claim 1, wherein the origin of replication comprises SeqID#12.
5. The synthetic mammalian expression plasmid of claim 1, wherein the ribosomal binding site ("RBS") comprises a prokaryotic RBS.
6. The synthetic mammalian expression plasmid of claim 1, wherein the ribosomal binding site ("RBS") comprises SeqID#13.
7. The synthetic mammalian expression plasmid of claim 1, wherein the polyadenylation signal ("PolyA") comprises a eukaryotic poly A signal.
8. The synthetic mammalian expression plasmid of claim 1, wherein the polyadenylation signal ("PolyA") comprises SeqID# 10.
9. The synthetic mammalian expression plasmid of claim 1, wherein the 5' UTR comprises a portion of a eukaryotic 5' UTR.
10. The synthetic mammalian expression plasmid of claim 1, wherein the 5' UTR comprises SeqID# 11.
11. The synthetic mammalian expression plasmid of claim 1, further comprising a prokaryotic promoter.
12. The synthetic mammalian expression plasmid of claim 11, wherein the prokaryotic promoter comprises PNEO and a transposon fragment ("Tn5").

13. The synthetic mammalian expression plasmid of claim 11, wherein the prokaryotic promoter comprises SeqID#14.
14. The synthetic mammalian expression plasmid of claim 1, wherein the selectable marker gene comprises SeqID#3.
15. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises at least one species specific codon modification.
16. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises a signal peptide.
17. The synthetic mammalian expression plasmid of claim 16, wherein the signal peptide is species specific.
18. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises a sequence that encodes a modified species specific growth hormone releasing hormone ("GHRH").
19. The synthetic mammalian expression plasmid of claim 1, further comprising a 5' untranslated region ("UTR") operatively linked to the first operatively-linked arrangement. .
20. The synthetic mammalian expression plasmid of claim 19, wherein the 5' untranslated region ("UTR") comprises a portion of a human growth hormone 5'UTR.
21. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises SeqID#4.
22. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises SeqID#5.

23. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises SeqID#6.

24. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises SeqID#7.

25. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises SeqID#8.

26. The synthetic mammalian expression plasmid of claim 1, wherein the codon optimized mammalian therapeutic gene sequence comprises SeqID#9.

27. A synthetic mammalian expression plasmid comprising SEQID#17.

28. A synthetic mammalian expression plasmid comprising SEQID#18.

29. A synthetic mammalian expression plasmid comprising SEQID#19.

30. A synthetic mammalian expression plasmid comprising SEQID#20.

31. A synthetic mammalian expression plasmid comprising SEQID#21.

32. A method for plasmid mediated gene supplementation comprising:  
delivering into a subject a codon optimized synthetic mammalian expression plasmid;  
wherein the codon optimized synthetic mammalian expression plasmid encodes a growth hormone releasing hormone ("GHRH") or functional biological equivalent in the subject.

33. The method of claim 32, wherein delivering into the cells of the subject the codon optimized synthetic mammalian expression plasmid is via electroporation.

34. The method of claim 32, wherein the cells of the subject are somatic cells, stem cells, or germ cells.

35. The method of claim 32, wherein the codon optimized synthetic mammalian expression plasmid consisting of SeqID#17, SeqID#18, SeqID#19, SeqID#20, and SeqID#21.

36. The method of claim 32, wherein the encoded GHRH is a biologically active polypeptide; and the encoded functional biological equivalent of GHRH is a polypeptide that has been engineered to contain a distinct amino acid sequence while simultaneously having similar or improved biological activity when compared to the GHRH polypeptide.

37. The method of claim 32, wherein the encoded GHRH or functional biological equivalent thereof facilitates growth hormone ("GH") secretion in the subject.